```
     FILE 'MEDLINE' ENTERED AT 11:15:18 ON 09 APR 2003
L1            22 S FGL2 OR FGL-2
L2         84655 S COAGULAT?
L3             7 S L2 AND L1
L4        483978 S REVIEW?
L5             1 S L1 AND L
L6             2 S L1 AND L4
L7            29 S FIBRINOGEN-LIKE PROTEIN
L8            40 S FIBRINOGEN-LIKE PROTEIN OR FGL-2 OR FGL2
L9            13 S L2 AND L8
L10           13 DUP REM L9 (0 DUPLICATES REMOVED)
L11           29 S LF-A1 OR LIVER FACTOR A1
L12            3 S L11 AND L2
L13       844552 S TISSUE?
L14            9 S L8 AND L13
L15            7 S FIBROLEUKIN
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14 ANSWER 5 OF 9 MEDLINE
ACCESSION NUMBER: 1999358396 MEDLINE
DOCUMENT NUMBER: 99358396 PubMed ID: 10429765
TITLE: The emerging role of immunoregulation of fibrinogen-related procoagulant **Fgl2** in the success or spontaneous abortion of early pregnancy in mice and humans.
AUTHOR: Clark D A; Ding J W; Chaouat G; Coulam C B; August C; Levy G A
CORPORATE SOURCE: Department of Medicine, McMaster University Hamilton, Ontario, Canada.
SOURCE: AMERICAN JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (1999 Jul) 42 (1) 37-43.
Journal code: 8912860. ISSN: 1046-7408.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991026
Last Updated on STN: 19991026
Entered Medline: 19991014

AB PROBLEM: Abortion of chromosomally normal embryos in the CBA X DBA/2 mating combination is triggered by release of Th1 cytokines (tumor necrosis factor [TNF]-alpha, interferon [IFN]-gamma, and interleukin [IL]-1), which cause abortion via a novel prothrombinase, **Fgl2**, and polymorphonuclear leukocytes. The site of activation may be maternal vascular endothelium on arteries and veins nourishing the placenta. Activation of coagulation is also prominent in spontaneous abortion of chromosomally normal human embryos. We asked where is **Fgl2** up-regulated in the uterus in murine abortions, and if similar **Fgl2** expression occurs in human pregnancy failure. METHODS: Control CBA X DBA/2 pregnant mice, or from mice injected with TNF-alpha + IFN-gamma on day 7.5 of gestation, were removed on day 8.5, fixed, sectioned, and subject to in situ hybridization for **Fgl2**. Sections were also stained for fibrin. Elective first trimester termination samples or biopsies taken early in the course of a recurrent miscarriage were similarly fixed, sectioned, and analyzed by in situ hybridization. Control and cytokine-treated mice were anticoagulated with heparin, an activator of antithrombin III, and/or the direct anti-thrombin inhibitor hirudin. RESULTS: Low level **Fgl2** expression localized to basal decidua remote from the embryo was noted in control mice; cytokine treatment, which causes greater than 80% of abortions, produced a striking up-regulation in this area as well as in a band at the junction of decidua and myometrium. Trophoblast also became strikingly positive. **Fgl2** expression was associated with increased fibrin staining. Anticoagulation significantly protected against abortions, but doses were limited by the complication of retroplacental hemorrhage. In **tissue** from normal first trimester pregnancy, minimal **Fgl2** positivity was seen in some villous syncytiotrophoblast, in villous stroma, cytotrophoblast, and in some cells in decidua. In spontaneous abortion of normal embryo, striking **Fgl2** positivity was seen in syncytiotrophoblast and extravillous cytotrophoblast, in association with areas of thrombus formation. CONCLUSIONS: **Fgl2** appears to be physiologically expressed and may protect against the internal danger of maternal and/or fetal bleeding during pregnancy and at parturition; a role in inhibiting transplacental traffic is also possible. External dangers in the form of stress, endotoxin, and antigens eliciting Th1 cytokine responses upregulate **Fgl2** prothrombinase in trophoblast as well as in decidua, which results in spontaneous abortion of immunogenetically "weaker" embryos.

L14 ANSWER 2 OF 9 MEDLINE
ACCESSION NUMBER: 2002487254 MEDLINE
DOCUMENT NUMBER: 22234700 PubMed ID: 12322892
TITLE: The same immunoregulatory molecules contribute to successful pregnancy and transplantation.
AUTHOR: Gorczynski Reginald M; Hadidi Sima; Yu Gary; Clark David A
CORPORATE SOURCE: Transplant Research Division, The Toronto Hospital, Ontario, Canada.. rgorczynski@uhnres.utoronto.ca
SOURCE: AMERICAN JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (2002 Jul) 48 (1) 18-26.
Journal code: 8912860. ISSN: 1046-7408.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20020927
Last Updated on STN: 20030130
Entered Medline: 20030129

AB PROBLEM: At least two dendritic cell-associated molecules have been shown to contribute to the successful outcome of organ and **tissue** allografts in mice, namely CD200 and MD-1. CD200 is up-regulated in rodent transplantation models where successful inhibition of rejection is accomplished, and is believed to signal immunosuppression following engagement of a receptor, CD200R, on macrophages and/or gammadelta T-cell receptor (gammadelta TCR+ cells MD-1 is implicated in controlling expression of costimulatory molecules including CD80/CD86 which induce an immunorejection response, and thus inhibition of MD-1 expression also facilitates increased graft survival MD-1 also stabilizes expression of CD14, part of the receptor complex for LPS. As well as the inhibition of rejection which follows blockade of MD-1 expression and/or augmentation of CD200 expression, an altered polarization in cytokine production is seen, with increased expression of interleukin-4 (IL-4), IL-10 and transforming growth factor-beta (TGF-beta), and decreased IL-2, interferon-gamma (IFN-gamma) and tumor nerosis factor-alpha (TNF-alpha). Successful pregnancy in allopregnant mice also depends upon control of graft rejection mechanisms. Proinflammatory T-helper 1 (Th1) cytokines (TNF-alpha + IFN-gamma + IL-1) have been shown to cause spontaneous abortion in mice by activating a novel prothrombinase, fibrinogen-like peptide (fibroleukin) **fgl2**, which may promote fibrin deposition in the graft rejection process; expression of IL-10, TGF-beta, and progesterone-induced blocking factor (PIBF) in contrast leads to lowering of abortion rates. Interestingly, the spontaneous abortion rates in abortion-prone CBA x DBA/2 matings and in the low abortion rate CBA x BALB/c matings were lower than the frequency of implantation sites showing fibrin(hi) + **fgl2** (mRNA)hi, implying regulation of the pro-abortion consequences of **fgl2** expression. METHODS: We have investigated, by in situ hybridization, CD200, MD-1 and **fgl2** expression in implantation sites in different strains of mice, and studied the effects of anti-MD-1, anti-CD200 and CD200Fc immunoadhesin on fetal and allograft survival. The role of indoleamine dioxygenase (IDO) was evaluated. RESULTS: CD200 mRNA expression occurred in the same sites as **fgl2** mRNA. Anti-CD200 antibody raised the abortion rate to predicted levels, and infusion of a CD200 immunoadhesin reduced the abortion rate, as did an anti-MD-1 antibody. The latter also improved organ and **tissue** graft survival. Suppression by antigen-presenting macrophages triggered by CD200 is dependent upon intact IDO activity. CONCLUSION: Regulation of CD200 and MD-1 expression may control both pregnancy and allograft survival.

L14 ANSWER 3 OF 9 MEDLINE
ACCESSION NUMBER: 2001393551 MEDLINE
DOCUMENT NUMBER: 21100908 PubMed ID: 11170750

10 ANSWER 2 OF 13 MEDLINE
ACCESSION NUMBER: 2002263883 MEDLINE
DOCUMENT NUMBER: 21990330 PubMed ID: 11994472
TITLE: Kinetic analysis of a unique direct prothrombinase, **fgl2**, and identification of a serine residue critical for the prothrombinase activity.
AUTHOR: Chan Camie W Y; Chan Matthew W C; Liu Mingfeng; Fung Laisum; Cole Edward H; Leibowitz Julian L; Marsden Philip A; Clark David A; Levy Gary A
CORPORATE SOURCE: Multi Organ Transplant Program, Toronto General Hospital and University of Toronto, 621 University Avenue 10th Floor, Room 116, Toronto, Ontario M5G 2C4, Canada.
SOURCE: JOURNAL OF IMMUNOLOGY, (2002 May 15) 168 (10) 5170-7. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020511
Last Updated on STN: 20020620
Entered Medline: 20020619

AB **fgl2** prothrombinase, by its ability to generate thrombin, has been shown to be pivotal to the pathogenesis of viral-induced hepatitis, cytokine-induced fetal loss syndrome, and xeno- and allograft rejection. In this study, the molecular basis of **fgl2** prothrombinase activity was examined in detail. Purified **fgl2** protein generated in a baculovirus expression system had no measurable prothrombinase activity, whereas the activity was restored when the purified protein was reconstituted into phosphatidyl-L-serine-containing vesicles. Reconstituted **fgl2** catalyzed the cleavage of human prothrombin to thrombin with kinetics consistent with a first order reaction, with an apparent V(max) value of 6 mol/min/mol **fgl2** and an apparent K(m) value for prothrombin of 8.3 microM. The catalytic activity was totally dependent on calcium, and factor Va (500 nM) enhanced the catalytic efficiency of **fgl2** by increasing the apparent V(max) value to 3670 mol/min/mol **fgl2** and decreasing the apparent K(m) value for prothrombin to 7.2 microM. By a combination of site-directed mutagenesis and production of truncated proteins, it was clearly shown that residue Ser(89) was critical for the prothrombinase activity of **fgl2**. Furthermore, **fgl2** prothrombinase activity was not inhibited by antithrombin III, soybean trypsin inhibitor, 4-aminobenzamidine, aprotinin, or phenylmethylsulfonyl fluoride, whereas diisopropylfluorophosphate completely abrogated the activity. In this work we provide direct evidence that **fgl2** cleaves prothrombin to thrombin consistent with serine protease activity and requires calcium, phospholipids, and factor Va for its full activity.

10 ANSWER 3 OF 13 MEDLINE
ACCESSION NUMBER: 1999358396 MEDLINE
DOCUMENT NUMBER: 99358396 PubMed ID: 10429765
TITLE: The emerging role of immunoregulation of fibrinogen-related procoagulant **Fgl2** in the success or spontaneous abortion of early pregnancy in mice and humans.
AUTHOR: Clark D A; Ding J W; Chaouat G; Coulam C B; August C; Levy G A
CORPORATE SOURCE: Department of Medicine, McMaster University Hamilton, Ontario, Canada.
SOURCE: AMERICAN JOURNAL OF REPRODUCTIVE IMMUNOLOGY, (1999 Jul) 42 (1) 37-43.
Journal code: 8912860. ISSN: 1046-7408.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991026
Last Updated on STN: 19991026
Entered Medline: 19991014

AB PROBLEM: Abortion of chromosomally normal embryos in the CBA X DBA/2 mating combination is triggered by release of Th1-cytokines (tumor necrosis factor [TNF]-alpha, interferon [IFN]-gamma, and interleukin [IL]-1), which cause abortion via a novel prothrombinase, **Fgl2**, and polymorphonuclear leukocytes. The site of activation may be maternal vascular endothelium on arteries and veins nourishing the placenta. Activation of **coagulation** is also prominent in spontaneous abortion of chromosomally normal human embryos. We asked where is **Fgl2** up-regulated in the uterus in murine abortions, and if similar **Fgl2** expression occurs in human pregnancy failure. METHODS: Control CBA X DBA/2 pregnant mice, or from mice injected with TNF-alpha + IFN-gamma on day 7.5 of gestation, were removed on day 8.5, fixed, sectioned, and subject to in situ hybridization for **Fgl2**. Sections were also stained for fibrin. Elective first trimester termination samples or biopsies taken early in the course of a recurrent miscarriage were similarly fixed, sectioned, and analyzed by in situ hybridization. Control and cytokine-treated mice were anticoagulated with heparin, an activator of antithrombin III, and/or the direct anti-thrombin inhibitor hirudin. RESULTS: Low level **Fgl2** expression localized to basal decidua remote from the embryo was noted in control mice; cytokine treatment, which causes greater than 80% of abortions, produced a striking up-regulation in this area as well as in a band at the junction of decidua and myometrium. Trophoblast also became strikingly positive. **Fgl2** expression was associated with increased fibrin staining. Anticoagulation significantly protected against abortions, but doses were limited by the complication of retroplacental hemorrhage. In tissue from normal first trimester pregnancy, minimal **Fgl2** positivity was seen in some villous syncytiotrophoblast, in villous stroma, cytotrophoblast, and in some cells in decidua. In spontaneous abortion of normal embryo, striking **Fgl2** positivity was seen in syncytiotrophoblast and extravillous cytotrophoblast, in association with areas of thrombus formation. CONCLUSIONS: **Fgl2** appears to be physiologically expressed and may protect against the internal danger of maternal and/or fetal bleeding during pregnancy and at parturition; a role in inhibiting transplacental traffic is also possible. External dangers in the form of stress, endotoxin, and antigens eliciting Th1 cytokine responses upregulate **Fgl2** prothrombinase in trophoblast as well as in decidua, which results in spontaneous abortion of immunogenetically "weaker" embryos.

ACCESSION NUMBER: 92218390 MEDLINE
DOCUMENT NUMBER: 92218390 PubMed ID: 1313796
TITLE: Liver-specific expression of the gene coding for human factor X, a blood **coagulation** factor.
AUTHOR: Miao C H; Leytus S P; Chung D W; Davie E W
CORPORATE SOURCE: Department of Biochemistry, University of Washington, Seattle 98195.
CONTRACT NUMBER: HL16919 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1992 Apr 15) 267 (11) 7395-401.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-L01675; GENBANK-L01676; GENBANK-L01677; GENBANK-M81357; GENBANK-M83679; GENBANK-M83680; GENBANK-M83681; GENBANK-M83724; GENBANK-X53708; GENBANK-X53709
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920529
Last Updated on STN: 19980206
Entered Medline: 19920512

AB Factor X is a vitamin K-dependent glycoprotein that plays an essential role in both the intrinsic and extrinsic pathways of blood **coagulation**. Studies on a recombinant lambda phage containing the 5'-flanking region of the human factor X gene showed that the factor X gene was linked to and was located at the 3' end of the factor VII gene: the initiation codon of the factor X gene was 2823 base pairs (bp) downstream from the polyadenylation site of the factor VII gene. This 2.8-kilobase intergenic region, and progressively deleted fragments of it, was fused to the chloramphenicol acetyltransferase gene, and transient expressions in HepG2 cells, human fibroblasts, and Chinese hamster ovary cells were measured. A liver-specific promoter element, FXP1-binding site, essential for hepatocyte-specific transcription was identified. This promoter sequence, further localized to -63 to -42 bp in DNase I footprint studies, was homologous to **LF-A1** or hepatic nuclear factor-4 recognition sequence and was equally functional in the normal and inverse orientations. FXP1 site bound to nuclear protein(s) from HepG2 cells and complex formation was partially abolished by the presence of duplex oligonucleotides containing **liver factor-A1** or hepatic nuclear factor-4-binding sequences. Two additional positive elements located upstream of the promoter region, spanning from -215 to -149 bp (FXP2 site), and -457 to -351 bp (FXP3 site), were also established by reporter gene assays.

ACCESSION NUMBER: 93176811 MEDLINE
DOCUMENT NUMBER: 93176811 PubMed ID: 8439561
TITLE: The 5' sequence of human factor XII gene contains transcription regulatory elements typical of liver specific, estrogen-modulated genes.
AUTHOR: Citarella F; Misiti S; Felici A; Aiuti A; La Porta C; Fantoni A
CORPORATE SOURCE: Dipartimento di Biopatologia Umana, Universita di Roma La Sapienza, Italy.
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1993 Feb 20) 1172 (1-2) 197-9.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-D13129; GENBANK-D13130; GENBANK-D13131; GENBANK-D13132; GENBANK-D13133; GENBANK-D13134; GENBANK-D13135; GENBANK-D13136; GENBANK-D13137; GENBANK-X67330
ENTRY MONTH: 199303
ENTRY DATE: Entered STN: 19930416
Last Updated on STN: 19950206
Entered Medline: 19930331

AB The human Factor XII gene codes for a serine proteinase synthesized in liver that activates both the **coagulation** and the fibrinolytic cascades. The nucleotide sequence analysis of a HincII-HincII 3129 bp fragment was performed showing that the FXII promoter region contains neither CAAT and TATA regulatory elements, nor GC islands, but revealing the presence of two tandemly repeated sequences in opposite orientation, two **LF-A1** elements typical of the liver specific genes and one estrogen responsive element, that substantiates the observation of Factor XII gene modulation by estrogens.

L12 ANSWER 1 OF 3 MEDLINE
ACCESSION NUMBER: 1999339944 MEDLINE
DOCUMENT NUMBER: 99339944 PubMed ID: 10411637
TITLE: Complete nucleotide sequence, origin of isoform and functional characterization of the mouse hepsin gene.
AUTHOR: Kawamura S; Kurachi S; Deyashiki Y; Kurachi K
CORPORATE SOURCE: Department of Human Genetics, University of Michigan Medical School, Ann Arbor 48109-0618, USA.
CONTRACT NUMBER: 5960AR20557 (NIAMS)
HL38644 (NHLBI)
MO1RR00042 (NCRR)
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (1999 Jun) 262 (3) 755-64.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990820
Last Updated on STN: 20000303
Entered Medline: 19990806

AB Hepsin, a type-II membrane-associated serine protease, has been implicated in cell growth and development as well as possible initiation of blood **coagulation**. Here, we report on the complete nucleotide sequence, functional characterization of key structural features and the promoter of the mouse hepsin gene. The gene has a size of approximately 17 kb, and is composed of 12, 13, or 14 exons depending on alternative intron splicings - one in the 5'-UTR and the other two in the second intron. The latter two, which occur in approximately half of the hepsin transcripts, generate a hepsin mRNA species with an extra exon, which is responsible for producing a hepsin isoform with a unique 20-residue sequence inserted in the cytoplasmic portion of hepsin. Most hepsin transcripts have the 5'-UTR intron spliced, and its splicing can occur independently of the other alternative splicings. The transcriptional initiation site was determined to be 636 bp upstream of the first ATG site in a cytidine-rich region. The 5'-flanking region of hepsin up to nucleotide 274 showed a substantial promoter activity in HepG2 cells, with its expression activity sevenfold higher in the presence of the 5'-UTR intron sequence in comparison to that without the intron sequence. The basal promoter region contains potential binding sites for several transcription factors including SP1, AP2, C/EBP, **LF-A1**, and E box, which may be responsible for ubiquitous, but liver- and kidney-preferred tissue expression of the hepsin gene.

L7 ANSWER 4 OF 7 MEDLINE
ACCESSION NUMBER: 1999245238 MEDLINE
DOCUMENT NUMBER: 99245238 PubMed ID: 10228554
TITLE: Antisense RNA **gene therapy** for studying and modulating biological processes.
AUTHOR: Weiss B; Davidkova G; Zhou L W
CORPORATE SOURCE: Department of Pharmacology, MCP Hahnemann University, Philadelphia, Pennsylvania 19129, USA.. weissb@auhs.edu
CONTRACT NUMBER: MH 42148 (NIMH)
SOURCE: CELLULAR AND MOLECULAR LIFE SCIENCES, (1999 Mar) 55 (3) 334-58. Ref: 164
Journal code: 9705402. ISSN: 1420-682X.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990519

AB Agents that produce their effects through an antisense mechanism offer the possibility of developing highly specific alternatives to traditional pharmacological antagonists, thereby providing a novel class of therapeutic agents, ones which act at the level of gene expression. Among the antisense compounds, antisense RNA produced intracellularly by an expression vector has been used extensively in the past several years. This **review** considers the advantages of the antisense RNA approach over the use of **antisense oligodeoxynucleotides**, the different means by which one may deliver and produce antisense RNA inside cells, and the experimental criteria one should use to ascertain whether the antisense RNA is acting through a true antisense mechanism. Its major emphasis is on exploring the potential therapeutic use of antisense RNA in several areas of medicine. For example, in the field of oncology antisense RNA has been used to inhibit several different target proteins, such as growth factors, growth factor receptors, proteins responsible for the invasive potential of tumor cells and proteins directly involved in cell cycle progression. In particular, a detailed discussion is presented on the possibility of selectively inhibiting the growth of tumor cells by using antisense RNA expression vectors directed to the individual calmodulin transcripts. Detailed consideration is also provided on the development and potential therapeutic applications of antisense RNA vectors targeted to the D2 dopamine receptor subtype. Studies are also summarized in which antisense RNA has been used to develop more effective therapies for infections with certain viruses such as the human immunodeficiency virus and the virus of hepatitis B, and data are **reviewed** suggesting new approaches to reduce elevated blood pressure using antisense RNA directed to proteins and receptors from the renin-angiotensin system. Finally, we outline some of the **problems** which the studies so far have yielded and some outstanding questions which remain to be answered in order to develop further antisense RNA vectors as therapeutic agents.

L7 ANSWER 5 OF 7 MEDLINE
ACCESSION NUMBER: 1998175844 MEDLINE
DOCUMENT NUMBER: 98175844 PubMed ID: 9516088
TITLE: **Antisense oligonucleotide** therapeutics for human leukemia.
AUTHOR: Gewirtz A M
CORPORATE SOURCE: Department of Pathology, University of Pennsylvania School of Medicine, Philadelphia 19104, USA.
SOURCE: CRITICAL REVIEWS IN ONCOGENESIS, (1997) 8 (1) 93-109. Ref: 131
Journal code: 8914610. ISSN: 0893-9675.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980520
Last Updated on STN: 19980520
Entered Medline: 19980508

AB The development of reliable gene disruption strategies, and their application in living cells, has proven to be an extraordinarily important advance for cell and molecular biologists. Using the various available approaches, the specific functions of any given gene may now be investigated directly in the relevant cell type. Application of similar experimental tools in a clinical setting might prove to be equally valuable and could well form the basis of a monumental advance in the practice of clinical medicine. This seems particularly true at the present time since much progress has been made in understanding the molecular pathogenesis of many diseases, including cancer. For these reasons a tremendous amount of interest has been generated in the use of oligodeoxynucleotides to modify gene expression. However, in spite of some notable successes which are detailed in this **review**, oligonucleotides have generated controversy in regards to their mechanism of action, reliability, and ultimate therapeutic utility. Nevertheless, the potential power of the "antisense" approach remains undisputed, and its ultimate therapeutic utility is far reaching. Accordingly, the **problems** associated with the use of these compounds are clearly worth solving. It remains the hope of many laboratories that the day will soon come when these techniques will make an important contribution to the management of CML and other neoplastic disorders.

L10 ANSWER 1 OF 13 MEDLINE
ACCESSION NUMBER: 2003083179 IN-PROCESS
DOCUMENT NUMBER: 22482708 PubMed ID: 12593995
TITLE: Cloning and tissue expression of the tissue prothrombinase **Fgl-2** in the Sprague-Dawley rat.
AUTHOR: Rychlik Daniel F; Chien Edward K; Wolff David; Phillippe Shiela; Phillippe Mark
CORPORATE SOURCE: Rinehart Center for Reproductive Medicine, Evanston, Illinois, USA.
SOURCE: JOURNAL OF THE SOCIETY FOR GYNECOLOGIC INVESTIGATION, (2003 Feb) 10 (2) 67-73.
Journal code: 9433806. ISSN: 1071-5576.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030221
Last Updated on STN: 20030221

AB To sequence and characterize the expression of the prothrombinase **Fgl-2** in the Sprague-Dawley rat.Reverse-transcriptase polymerase chain reaction was performed on RNA from spontaneously cycling adult pregnant Sprague-Dawley rats by using specific **Fgl-2** primers. The resulting amplicon was also used to screen a rat spleen bacteriophage library and to probe a Northern blot of various tissues. The rat **Fgl-2** amino acid sequence was compared with the known sequences in mouse and human.**Fgl-2**-specific amplicon bands were observed in the rat brain, kidney, liver, ovary, spleen, and gestational day 22 and postpartum uterus. The rat **Fgl-2** cDNA and amino acid sequence were found to be homologous with those of human (86% and 74%, respectively) and mouse (91% and 87%, respectively). Northern blotting demonstrated two different-sized transcripts (1.3 and 3.4 kb), and expression was observed in the cervix, heart, liver, ovary, and nongestational and gestational day 22 myometrium.Thrombin is classically generated from the cleavage of the proenzyme prothrombin by activated factors V and X. In tissues thrombin appears to be generated by a novel prothrombinase **Fgl-2** (**fibrinogen-like protein**) whose activity is stimulated by proinflammatory mediators. **Fgl-2** provides the mechanistic coupling between proinflammatory cytokines and the generation of active thrombin independent of the **coagulation** cascade. Our studies confirmed the expression of **Fgl-2** mRNA in several rat tissues, including the pregnant uterus, where it could play a key role in the initiation of parturition especially in response to local or systemic infection.

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     FILE 'MEDLINE' ENTERED AT 10:57:01 ON 16 APR 2003
L7          4242 S ANTISENSE OLIGONUCLEOTID?
L8          3936 S TARGET? AND STABILITY
L9            83 S L7 AND L8
L10       484259 S REVIEW?
L11           10 S L9 AND L10
L12       389303 S PROBLEM?
L13            3 S L7 AND L8 AND L12
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FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:20:51 ON 07 APR 2003

L1	80	S	FGL2 OR FGL-2
L2	22	S	IMMUNE COAGULAT?
L3	175034	S	COAGULAT?
L4	18	S	L1 AND L3
L5	10	DUP REM	L4 (8 DUPLICATES REMOVED)
		E	LEVY G/AU
L6	2087	S	E3
		E	LEVY GARY/AU
L7	88	S	E3 OR E4 OR E5 OR E6 OR E7
L8	2175	S	L6 OR L7
L9	32	S	L1 AND L8
L10	25	DUP REM	L9 (7 DUPLICATES REMOVED)
L11	295042	S	HEPATITIS
L12	20	S	L10 AND L11
L13	65917	S	HBV OR HCV
L14	0	S	L12 AND L13
L15	4502573	S	PREVENT? OR INHIBIT?
L16	5	S	L15 AND L12
L17	5	DUP REM	L16 (0 DUPLICATES REMOVED)
L18	33	S	L1 AND L15
L19	17	DUP REM	L18 (16 DUPLICATES REMOVED)
L20	8	S	L2 AND L15
L21	6	DUP REM	L20 (2 DUPLICATES REMOVED)
L22	0	S	L13 AND L2
L23	259	S	L3 AND L13
L24	0	S	L23 AND L1
L25	57	S	L23 AND L15
L26	41	DUP REM	L25 (16 DUPLICATES REMOVED)

L Number	Hits	Search Text	DB	Time stamp
1	60	levy-g.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/04/07 14:07
3	0	levy-g.in. and fgl2	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/04/07 14:07
4	2	levy-gary.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/04/07 14:07
2	6	fgl2	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/04/07 14:10
5	18	fgl2 or fgl?2	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2003/04/07 14:10

FILE 'MEDLINE' ENTERED AT 11:42:55 ON 26 JUN 2002

L1	8	S	IMMUNE COAGULATION
L2	4	S	L1 AND HEPATITIS
L3	0	S	HBV AND L1
L4	0	S	FGL2 AND HBV
L5	202	S	NUCLEOCAPSID AND HBV
L6	37	S	INHIBIT? AND L5
L7	2	S	ANTISENSE AND L6
L8	0	S	L1 AND L5
L9	1889	S	CORE AND HBV
L10	151	S	INHIBIT? AND L9
L11	0	S	ANRTISENSE AND L10
L12	11	S	ANTISENSE AND L10
L13	663	S	PROTHROMBINASE
L14	19637	S	HBV OR HCV
L15	0	S	L13 AND L14
L16	1	S	HFGL2
L17	2	S	FULMINANT AND L1
L18	1617266	S	INHIBIT? OR PREVENT?
L19	4	S	L1 AND L18
L20	54	S	HEPATITIS AND (NUCLEOCAPSID OR CORE) AND ANTISENSE
L21	54		DUP REM L20 (0 DUPLICATES REMOVED)
L22	54	S	L21
L23	0	S	L1 AND L21
L24	54	S	L21
L25	32	S	L18 AND L21
L26	28	S	LF-A1
L27	10431	S	HBV OR HVC
L28	19637	S	HBV OR HCV
L29	0	S	L26 AND L28

FILE 'MEDLINE' ENTERED AT 11:42:55 ON 26 JUN 2002

L1	8	S	IMMUNE COAGULATION
L2	4	S	L1 AND HEPATITIS
L3	0	S	HBV AND L1
L4	0	S	FGL2 AND HBV
L5	202	S	NUCLEOCAPSID AND HBV
L6	37	S	INHIBIT? AND L5
L7	2	S	ANTISENSE AND L6
L8	0	S	L1 AND L5
L9	1889	S	CORE AND HBV
L10	151	S	INHIBIT? AND L9
L11	0	S	ANRTISENSE AND L10
L12	11	S	ANTISENSE AND L10
L13	663	S	PROTHROMBINASE
L14	19637	S	HBV OR HCV
L15	0	S	L13 AND L14
L16	1	S	HFGL2
L17	2	S	FULMINANT AND L1
L18	1617266	S	INHIBIT? OR PREVENT?
L19	4	S	L1 AND L18
L20	54	S	HEPATITIS AND (NUCLEOCAPSID OR CORE) AND ANTISENSE
L21	54		DUP REM L20 (0 DUPLICATES REMOVED)
L22	54	S	L21
L23	0	S	L1 AND L21
L24	54	S	L21
L25	32	S	L18 AND L21

L Number	Hits	Search Text	DB	Time stamp
1	2	hepatitis and fgl-2	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/06/26 10:46
2	6	(prevent$3 or reduc$4) and (immune adj coagulation)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/06/26 10:52
3	2	(antisense adj oligonucleotide) and fgl2	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/06/26 10:55
4	2	(antisense adj oligonucleotide) with hepatitis and (N adj protein)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/06/26 10:53
5	2	(antisense adj oligonucleotide) and (immune adj coagulat$3)	USPAT; US-PGPUB; EPO; JPO; DERWENT; IBM_TDB	2002/06/26 10:55